## ABSTRACT OF THE DISCLOSURE

The presence of the ancient anti-inflammatory peptide α-melanocyte stimulating hormone (α-MSH [1-13], SYSMEHFRWGKPV) in barrier organs such as gut and skin suggests a role in the nonspecific (innate) host defense system. α-MSH and other amino acid sequences derived from α-MSH were determined to have antimicrobial influences, including against two major and representative cutaneous and mucosal pathogens: *Staphylococcus aureus* and *Candida albicans*. α-MSH peptides had antimicrobial effects against *S. aureus* and significantly reversed the enhancing effect of urokinase on *S. aureus* colony formation. α-MSH and other amino acid sequences reduced *C. albicans* viability and germination. α-MSH peptides also enhanced *C. albicans* killing by human neutrophils. The antimicrobial agent is selected from the group consisting of one or more peptides including the amino acid sequence KPV, one or more peptides including the amino acid sequence MEHFRWG, or a biologically functional equivalent of any of the foregoing. The most effective of the peptides were those bearing the C-terminal amino acid sequence of α-MSH, i.e., α-MSH (1-13), (6-13), and (11-13). The α-MSH "core" sequence (4-10), important for melanotropic effects, was also effective but significantly less potent. Antimicrobial influences of α-MSH peptides could be mediated by their well-known capacity to increase cellular cAMP; this messenger was significantly augmented in peptide-treated yeast. α-MSH has potent anti-inflammatory effects and is expected to be useful for treatment of inflammation in human and veterinary disorders. Reduced killing of pathogens is a detrimental consequence of therapy with corticosteroids and nonsteroidal anti-inflammatory drugs during infection. Therefore, anti-inflammatory agents based on α-MSH peptides that do not reduce microbial killing, but rather enhance it, would be very useful. The antimicrobial effects of these α-MSH peptides occurred over a broad range of concentrations including the physiological (picomolar) range.